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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

SERIAL NO.:	08/160,965	§	DOCKET: D-5880
FILING DATE:	12/02/93	§	EXAMINER: SIDBERRY, H.
APPLICANT:	JAMES M. MUSSER, ET AL.	§	GR ART UNIT: 1813
TITLE:	VACCINES CONTAINING CYSTEINE PROTEASE AND METHODS TO PROTECT AGAINST GROUP A STREPTOCOCCI	§	

#24 SB 10/16/96 (AF)

Box AF
Commissioner of Patents and Trademarks
Washington, D.C. 20231

RESPONSE

Dear Sir:

Responsive to the Office Action of April 3, 1996, applicants respectfully request consideration of the following remarks and reconsideration of the rejections in light of such remarks.

ISSUES

Outstanding Issues include:

- Objection to the drawings
- The objection to the specification and rejection of the claims under 35 U.S.C. § 112, first paragraph.
- Rejection of claims 1 to 4 under 35 U.S.C. § 102b or 103.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231 on 10/3/96
Thomas D. Paul
Thomas D Paul 10/8/96
Signature Date

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Rejection of claims 1-4, 6-17 under 35 U.S.C. § 103.

Rejection of claims 1-4 under 35 U.S.C. § 102(a/b).

Rejection of claims 5-17 under 35 U.S.C. § 103.

Object to the Drawings

Applicants respectfully request that this objection be held in abeyance until the claims have been allowed, at which time applicants will submit formal drawings.

35 U.S.C. § 112(1)

The specification is objected to and the claims are rejected under 35 U.S.C § 112, first paragraph as failing to provide an enabling disclosure. Applicants believe that in light of the affidavit submitted with the last response and the specification the application and the claims are is enabled. This is especially true in light of recent Federal Circuit decisions and opinions from the Commissioner. It is not the applicant's obligation to provide FDA type data or appropriate injection schemes that would satisfy FDA requirements.

Applicants assert that sufficient information is provided in the Examples in the specification, as well as, in the affidavits attached to the last response. This affidavit was by one of the inventors, James M. Musser, and showed that the claimed invention is operative and demonstrates that the method as claimed operates to protect against streptococcal infection. Applicant asserts that the requirements for specific examples of *in vivo* use in humans are not appropriate in light of the Commissioner's guidelines and the Federal Circuit's opinion. *In re*

Brana, 51 F.3d 1560 (Fed. Cir. 1995). The Patent Office is not an FDA regulatory agency. The facts that the affidavits and the Example section of a specification clearly show that it works and is effective in an animal meets the requirements as specified by the court. The specific protocol for humans as well as specific concentration are more appropriate for approval under FDA rules and regulations rather than the Patent Office. One skilled in the art readily recognizes, given the guidance provided in the specification and affidavit attached to the last response that the method works at providing protection against streptococcus infection. If the applicants teach the public that the method works and shows some desirable pharmaceutical property, they have made a significant and useful contribution to the art, even though it may eventually appear that this method is without value in the treatment in humans. *In re Brana*, 51 F.3d 1560 (Fed. Cir. 1995). Because applicant has shown the pharmaceutical property claimed in the specification and affidavit, this rejection should be withdrawn.

35 U.S.C. § 102(b).

Claims 1 to 4 are rejected on 35 U.S.C. § 102(b) as anticipated by or in the alternative under 35 U.S.C. § 103 is obvious over Björck, et al.

Applicants respectfully submit that the rejections of claims 1-4 as anticipated by Björck et al. are based upon a mischaracterization of the Björck et al. compound. Applicants respectfully request that the abstract be reread. Björck et al. clearly state that their compounds mimic the proposed binding centre of "cystatin C". Cystatin C is not a cysteine protease, but rather is an inhibitor present in

extracellular fluids. Applicants' claims are directed to a vaccine that contains a conserved cysteine protease--an inhibitor of this compound is clearly not the same as the compound.

The Björck et al. compound has absolutely nothing in common with the compounds used in the Applicants' claimed vaccines and methods. It shares no part of its amino acid sequence with the cysteine protease compounds utilized in Applicants' claimed vaccines. Anticipation requires that the claimed invention and the reference disclosure be identical. Here, there is no similarity between the claimed invention and the reference disclosure. They are different compounds. The tripeptide described by Björck et al. is not found anywhere in the amino acid sequence of the cysteine protease used in Applicants' claimed compositions. This would be expected since the peptide is a derivative of cystatin C not cysteine protease. Therefore, Applicants respectfully request withdrawal of these rejections.

35 U.S.C. § 103.

Claims 1-4 and 6-17 are rejected over Björck et al., in view of Kehoe and Fischetti, et al.

As discussed above, this rejection is based on a mischaracterization of the Björck et al. peptide as a derivative of a cysteine protease. Careful reading of Björck shows that the peptide is a derivative of a different compound cystatin C. Applicants' claims are directed to the use of a cysteine protease as a vaccine. Since Björck et al. do not describe a cysteine protease derivative, the reference cannot suggest the use of a cysteine protease as a vaccine.

Furthermore, Björck et al. teach away from Applicants' invention. Björck et al. found that a cysteine protease inhibitor suppressed *S. pyogenes* growth *in vitro* and thus protected mice from lethal bacterial infection. In other words, according to the Björck et al. results, a decrease in cysteine protease activity is associated with a favorable pharmacological result. The claims of Applicants on the other hand require that more cysteine protease be used. This is the exact opposite of what the Björck et al. reference suggests to those of skill in the art.

Since Björck also teaches a different compound it cannot suggest that another compound would be useful. Therefore, applicants respectfully request withdrawal of this rejection.

35 U.S.C. § 102(a/b).

Claims 1-4 are rejected under 35 U.S.C. § 102(a/b) as anticipated by Kapor or Tal or Hauser or Gerlach. Applicants assert that none of these references teach a vaccine. They teach purification procedures. Further, there is no indication the dialysis procedure described yields a nontoxic carrier, and no indication that such compound will yield a vaccine. In addition, the limitation that the vaccine compositions contain a physiologically acceptable vehicle in addition to the cysteine protease is ignored. The CCPA has held that "absent a disclosure by [the cited prior art] of specific therapeutic or pharmaceutical uses for [a known compound], the addition of a pharmaceutical carrier to that compound and the determination of suitable dosage forms is not obvious." *In re Anthony*, 162 USPQ 594, 597 (CCPA 1969). Further, the claim requires that a conserved cysteine protease be present in

an amount sufficient to confer immunity to group A streptococcal infection. None of the cited references describe either the conserved cysteine protease in combination with the physiologically acceptable vehicle, or a composition comprising the conserved cysteine protease in the specified amount. These limitations are not obvious variants of the cysteine proteases described in the cited prior art.

None of the references provide motivation to administer cysteine protease to a human or animal. Thus, there is no motivation in the cited prior art to incorporate the cysteine protease into pharmaceutically acceptable carriers in amounts sufficient to induce immunity against group A streptococci.

Thus, Applicants respectfully request withdrawal of the rejection.

35 U.S.C. § 103.

Claims 5-17 are rejected as unpatentable over Gerlach et al. or Hauser in view of Kehoe et al and Fischetti et al and Abe et al and Kapor et al.

The claims of the present invention all require a conserved cysteine protease in an amount sufficient to induce immunity to group A streptococci, and a physiologically acceptable non-toxic vehicle.

As the Patent Office admits, Gerlach and Hauser do not use cysteine protease. Further Kehoe, Fischetti and Kapor do not teach using cysteine proteases as vaccines or in methods of vaccination. Since there has been a long felt need to have a vaccine, Applicants are confused as to how references which do not teach or suggest that cysteine protease is useful for this purpose can teach that they solve this long felt need. Indeed, in seven decades of research into vaccines against group

A streptococci, no persons other than the present Applicants have suggested the use of a streptococcal cysteine protease as a vaccine. It is difficult to imagine a more clear-cut case of non-obviousness.

Therefore, Applicants respectfully request that these grounds of rejection be withdrawn.

Applicants do not believe that there are any fees due with this response. If any fees are due over, please charge them to account number 06-2375, Order No. 957111 from which the undersigned is authorized to withdraw.

Applicants assert that in view of the remarks the application is now in condition for allowance. Accordingly, applicants respectfully request that Letters of Patent be issued and the application herein admitted. For any problems, applicants respectfully request that the examiner contact the undersigned at 713/651-5325 for a quick resolution of the problem.

Respectfully submitted,

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Date: 10/3/96

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